UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/476,275	06/07/95	ANDERSON	D 012712-155

EXAMINER
SCHWADRON, R

ART UNIT	PAPER NUMBER
1816	13

18N1/0624

E. JOSEPH GESS
BURNS DOANE SWECKER & MATHIS
P O BOX 1404
ALEXANDRIA VA 22313-1404

DATE MAILED: 06/24/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

5/2/96
3/21/96

☒ This application has been examined ☒ Responsive to communication filed on 1/4/96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1, 2, 4, 5, 19-28 are pending in the application.
   Of the above, claims none are withdrawn from consideration.
2. ☒ Claims 3, 6-18 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1, 2, 4, 5, 19-28 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. Claims 1,2,4,5,19-28 are under consideration. Claims 25-28 are newly added.

RESPONSE TO APPLICANT'S ARGUMENTS

16. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1,2,4,5,19-28 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9 of copending application Serial

No. 08/478967. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. Claim 20 is included as reading on claim 18, not 8, because the antibody of claim 20 is not recited in the method of claim 8. While claims 6-9 differ in scope from claims 1,4,5,21-24 in that claims 6-9 encompass certain specific combinations of antibodies not recited in claims 1,4,5,21-24, both sets of claims encompass the treatment of B cell lymphoma using antibody derived from transfectoma ATCC 69119. While claims 6-9 differ in scope from claims 19 and 20 in that claims 6-9 encompass certain specific combinations of antibodies not recited in claims 19 and 20, both sets of claims encompass the treatment of B cell lymphoma using antibody derived from transfectoma ATCC 69119 and HB 11388. The dosages and time schedule for administration of the aforementioned antibodies are overlapping in the two sets of claims. It would have been obvious to a routineer that the method of treatment using an antibody could have been combined with conventional chemotherapeutic agents in order to increase the efficacy of treatment. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.
This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant has indicated in the amendment filed 3/21/96 that a terminal disclaimer will be submitted upon an indication that the claimed subject matter is otherwise allowable.

18. Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 18 of copending application Serial No. 08/475,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Claims 19 and 20 differ in scope from claim 18

in that claim 18 specifies a specific species for each antibody in the claim, while claims 19 and 20 only specify a species for one of the antibodies recited in the claim. However, both sets of claims read on the use of chimeric antiCD20 antibody followed by the use of radiolabelled antiCD20 antibody. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant has indicated in the amendment filed 3/21/96 that a terminal disclaimer will be submitted upon an indication that the claimed subject matter is otherwise allowable.

19. The use of the trademarks MILLI-Q AND ALCONOX has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicants arguments in the amendment received 3/21/96 have been considered and deemed not persuasive.

20. Regarding the Reff declaration filed 1/4/96 the following comments are made. The Reff declaration appears to establish that the additional nucleotide in Figure 2D was an error and that the appropriate sequence was known as per Sequence Id no. 1. Regarding applicants comments about submitting a new sequence listing, the Reff declaration establishes that Sequence Id no. 1 is correct, so that it is unclear as to why a new Seq. ID. listing would be needed.

21. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to for the reasons discussed in paragraph 23 sections A and B of the Office Action mailed 12/21/95.

22. Claims 1,2,4,5,19-28 stand rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification. Applicants arguments have been considered and deemed not persuasive.

While the aforementioned hybridoma and transfectoma have been deposited with the ATCC under conditions of the Budapest Treaty, applicants need to supply the date that ATCC 69119 was deposited with the ATCC, and meet the requirements under 37 CFR 1.808. The requirements under 37 CFR 1.808 can be met by submission of an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Regarding applicants statement in the amendment filed on 3/21/96, page 4, penultimate paragraph, it is unclear as to what

"will be made irrevocably available" means. A preferred statement is "that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent". The statement should also indicate that it applies to the instant application. Applicant also needs to amend the specification to indicate the date that the ATCC 69119 was deposited with the ATCC.

23. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

24. Claims 19 and 20 remain rejected under 35 U.S.C. § 103 as being unpatentable over Grossbard in view of Anderson et al. for the reasons elaborated in paragraph 26 of the Office Action mailed 12/21/95. Applicants arguments in pages 5-9 of the amendment filed 3/21/96 have been considered and deemed not persuasive. In view of the fact that murine antiCD20 had been used for the treatment of B cell lymphoma, it would have been obvious to a routineer that a chimeric antiCD20 antibody could have been used for treating B cell lymphomas based on the art known advantages of chimeric over murine

antibodies. A routineer would have used a chimeric antibody in combination with a radiolabelled murine antibody because Grossbard et al. teach that radiolabelled chimeric antibodies would be therapeutically inferior to radiolabelled murine antibodies because "prolonged serum half-life of humanized RAbs may result in a substantial increase in nonspecific total body irradiation."(page 873, first column, last paragraph). Regarding applicants comments on page 6 of the instant amendment, Table 6 of Grossbard demonstrates that a variety of different antiCD20 antibodies have already been used successfully for the treatment of human disease. Regarding the IDEC press release submitted with the instant amendment, Grossbard et al. teach that similar results were achieved in clinical trials using radiolabelled antiCD20 murine antibody (see Table 6, first column). Regarding applicants comments on pages 6-8 of the instant amendment, the Anderson declaration submitted 3/21/96 seems to indicate that the claimed chimeric antibody was not available other than to the authors of the Anderson et al. publication. However, the M.P.E.P. in section 2132, part (c) (2100-47, Rev. 1, Sept. 1995) indicates that the "by others" clause of 35 U.S.C. § 102(a) means "any combination of authors or inventors different than the inventive entity". Therefore, the Anderson et al. abstract is prior art in that it was known by others (eg. the noninventor authors of the Anderson et al. publication). Applicant is advised that this rejection can be overcome by a Katz type declaration.

25. Claims 1,2,4,5,21-28 stand rejected under 35 U.S.C. § 103 as being unpatentable over Robinson et al. (WO 88/04936) in view of Anderson et al. for the reasons elaborated in paragraph 27 of the Office Action mailed 12/21/95. Applicants arguments in page 9 of the amendment filed 3/21/96 have been considered and deemed not persuasive. Regarding the IDEC press release submitted with the instant amendment, Table 6 of Grossbard demonstrates that a variety of different antiCD20 antibodies have already been used

successfully for the treatment of human disease. Furthermore, Robinson et al. teach that, "the inclusion of appropriate human immunoglobulin sequences can result in an antibody which efficiently interacts with human effector cells in vivo to cause tumor cell lysis and the like."(page 3, last paragraphs). Thus, a routineer would have expected that a chimeric version of a murine antibody would show superior in vivo efficacy. Regarding applicants comments on page 9 of the instant amendment, the Anderson declaration submitted 3/21/96 seems to indicate that the claimed chimeric antibody was not available other than to the authors of the Anderson et al. publication. However, the M.P.E.P. in section 2132, part (c) (2100-47, Rev. 1, Sept. 1995) indicates that the "by others" clause of 35 U.S.C. § 102(a) means "any combination of authors or inventors different than the inventive entity". Therefore, the Anderson et al. abstract is prior art in that it was known by others (eg. the noninventor authors of the Anderson et al. publication). Applicant is advised that this rejection can be overcome by a Katz type declaration.

OTHER REJECTIONS

26. Claims 19 and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 20 are indefinite in that they depend on cancelled claim 18. The claims need to incorporate the limitations recited in cancelled claim 18.

27. Claims 1,2,4,5,21-28 are rejected under 35 U.S.C. § 103 as

being unpatentable over Robinson et al. (US Patent 5,500,362).

The claims are drawn to a method of treating B cell lymphoma. Robinson et al. teach a chimeric antiCD20 antibody which contains a human IgG1 heavy chain constant region and a human light chain constant region(see claim 1). The antigen bound by the hybridoma HB9303 is CD20 (see column 7, penultimate paragraph and column 20, second paragraph). Robinson et al. teach that chimeric antibody contains a human K light chain constant region (see column 17, penultimate paragraph). Robinson et al. teach that said antibody is immunologically active (eg. mediates ADCC and CDC, see claims 2 and 3). Robinson et al. teach that chimeric antiCD20 antibodies can be used in vivo for the treatment of B cell lymphoma(see column 19, paragraphs 4). The species of antibody recited in the claim is encompassed by the generic antibody taught by Robinson et al., but Robinson et al. do not teach the particular claimed species of chimeric antiCD20 used in the claimed method. There appears to be no functional difference between the chimeric antibody of claim 1 of Robinson et al. and the antibody of the instant invention. The specification discloses that "all cell lines which are functionally equivalent are within the scope of the invention"(column 20, third paragraph). In addition, based on the disclosure of Robinson et al., a routineer would have produced the antibody of the instant invention or a functional equivalent using routine experimentation. It would have been obvious to a routineer that such a chimeric antibody would be administered in an art known pharmaceutically acceptable carrier, because said antibody was to be administered to humans. A routineer would have arrived at the concentration of antibody specified in the claims and time schedule of administration by routine experimentation. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Robinson et al. teach chimeric antiCD20 antibodies, and that said antibodies can be used be used for diagnostic and therapeutic purposes (see column 13, columns 2 and 3). A routineer

would have used antiCD20 antibodies in combination with any art known chemotherapeutic agent that had already been used to treat tumors.

28. Claims 1,2,4,5,21-28 are rejected under 35 U.S.C. § 103 as being unpatentable over Robinson et al. (WO 88/04936).

The claims are drawn a method of treating B cell lymphoma. Robinson et al. teach a chimeric antiCD20 antibody which contains heavy chain and light chain constant regions of human origin (see claim 17). Robinson et al. teach that chimeric antibody contains a human K light chain constant region and human IgG1 heavy chain constant region(see pages 37, last paragraph and page 38, second paragraph). Robinson et al. teach that said antibody is immunologically active (eg. mediate ADCC and CDC, see claims 28 and 29). Robinson et al. teach that chimeric antiCD20 antibodies can be used in vivo for the treatment of B cell lymphoma (see page 42, first paragraph). The claimed species of antibody is encompassed by the generic antibody taught by Robinson et al., but Robinson et al. do not teach the particular claimed species of chimeric antiCD20 antibody used in the claimed method. There appears to be no functional difference between the chimeric antibody of claim 17 of Robinson et al. and the antibody of the instant invention. Robinson et al. teach that "all cell lines which are functionally equivalent are within the scope of the invention"(page 44). In addition, based on the disclosure of Robinson et al., a routineer would have produced the antibody of the instant invention or a functional equivalent using routine experimentation. It would have been obvious to a routineer that such a chimeric antibody would be administered in an art known pharmaceutically acceptable carrier (eg. as per claim 22), because said antibody was to be administered to humans. A routineer would have arrived at the concentration of antibody specified in the claims and time schedule of administration by routine experimentation. It would have been prima facie obvious to one of ordinary skill in the art at the time the

invention was made to have created the claimed invention because Robinson et al. teach chimeric antiCD20 antibodies, and that said antibodies can be used be used for diagnostic and therapeutic purposes (see page 28, last paragraph continued on page 29 and page 29, first paragraph). A routineer would have used antiCD20 antibodies in combination with any art known chemotherapeutic agent that had already been used to treat tumors.

29. Claims 19 and 20 are rejected under 35 U.S.C. § 103 as being unpatentable over Robinson et al. (US Patent 5,500,362) or Robinson et al. (WO 88/04936) as applied to claims 1,2,4,5,21-28 above and further in view of Grossbard et al.

Regarding priority for the instant application with regards to prior art, the claimed invention is not disclosed in parent application 07/978891 and therefore priority for the instant application for the purpose of applying prior art is parent application 08/149099. Claim 20 is included as reading on claim 18, not 8, because the antibody of claim 20 is not recited in the method of claim 8. The claims are drawn to a method of treating B cell lymphoma with the antibodies recited in the claims. Robinson et al. (US Patent 5,500,362) or (WO 88/04936) make obvious the use of the claimed chimeric antiCD20 antibody to treat B cell lymphoma, but do not teach the claimed method.

Grossbard et al. teach that unconjugated murine antiCD20 antibody was used for the treatment of B cell lymphoma (see Table 2).Grossbard et al. teach that radiolabelled antiCD20 antibody was used for the treatment of B cell lymphoma (see Table 6). Grossbard et al. teach the use of unlabelled antibody, followed by radiolabelled antibody for the treatment of human lymphomas (see page 874, second column, last paragraph). In view of the fact that murine antiCD20 had been used for the treatment of B cell lymphoma, it would have been obvious to a routineer that a chimeric antiCD20 antibody could have been used for treating B cell lymphomas based on the art known advantages of chimeric over murine antibodies. A

routineer would have used a chimeric antibody in combination with a radiolabelled murine antibody because Grossbard et al. teach that radiolabelled chimeric antibodies would be therapeutically inferior to radiolabelled murine antibodies because "prolonged serum half-life of humanized RAbs may result in a substantial increase in nonspecific total body irradiation."(page 873, first column, last paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of the cited references to produce the method of the instant invention because Grossbard teaches the use of unlabelled antibody, followed by radiolabelled antibody for the treatment of human lymphomas and Grossbard et al. teach that radiolabelled chimeric antibodies would be therapeutically inferior to radiolabelled murine antibodies because "prolonged serum half-life of humanized RAbs may result in a substantial increase in nonspecific total body irradiation."(page 873, first column, last paragraph).

30. No claim is allowed.

31. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7939.

32. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ms Christina Chan can be reached on (703) 308-3973.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PATENT EXAMINER
GROUP 1800

Ron Schwadron, Ph.D.
Patent Examiner
Art Unit 1816
June 22, 1996